Chest Pain in Association with Pulmonary Hypertension

Its Similarity to the Pain of Coronary Disease

By William N. Viar, M.D., and T. R. Harrison, M.D.

This communication deals with a type of chest pain which is not uncommon, and which is likely to lead to an erroneous diagnosis of coronary arterial disease. The term "hypocyanotic angina," which has been applied to the syndrome in the past, is unfortunate because many of the patients are not cyanotic, and further because the physiologic mechanism of the pain, while still obscure, appears to be different from that of the pain of angina pectoris. In the patients we have observed, the one constant feature other than pain has been clinical evidence of increased pressure in the pulmonary vascular circuit. Hence, the term "pulmonary hypertensive pain" is employed, but with the reservation that more complete knowledge of the exact pathogenesis may make a different name desirable.

PULMONARY hypertensive pain may resemble angina pectoris not only as regards location, radiation, intensity, and quality of the discomfort, but also as regards the tendency to be initiated by physical exertion. In some patients the pain may be associated with outspoken electrocardiographic changes. (See figures 1 and 2.) Therefore, the diagnosis of myocardial infarction is likely to be made. The differentiation, while occasionally almost impossible, can usually be made with accuracy if one is familiar with the various clinical features of the syndrome.

In 1942 Burgess and Ellis wrote an excellent review article on chest pain in patients with mitral stenosis. They referred to Nothnagel's publication on the same subject, and summarized the more important papers dealing with angina-like pain in various disorders of the pulmonary vessels. Thus Vaquez and Giroux described the clinical findings of angina pulmonaire hypocyanotique associated with pulmonary arteriosclerosis. Posselt cited chest pain (dyspragia intermittens angiosclerotica pneumonalis) as one of the criteria for the diagnosis of pulmonary arteriosclerosis. Frugoni contrasted dolor pallidus of angina brought on by effort with dolor caeruleus seen in patients with pulmonary arterial disease. Other publications dealing with chest pain in relation to pulmonary arteriosclerosis include those of Arrillaga, Engelen, Brenner, and Brill and Krygier.

Pain resembling that of angina pectoris in patients with mitral stenosis was clearly described by Nothnagel. Sternberg reported autopsy findings of a patient with mitral stenosis who before death experienced severe pain of this type. The coronary arteries were described as being thin and widely patent. Parker and Weiss stated that pain and cyanosis were frequent symptoms of mitral stenosis when there were secondary pulmonary changes, and that these same symptoms were usually absent when such secondary changes were lacking.

In recent years there has been much interest in the subjects of anticoagulant therapy and thromboembolic disease. Compared to the numerous papers dealing with the electrocardiographic changes associated with pulmonary embolism, there have been relatively few reports in which the pain produced by the disorder has been carefully described. McGinn and White reported that most patients with pulmonary embolism complained initially of dyspnea and substernal oppression. They also re-
ferred to another type of pain which appeared later, and was always associated with pleural involvement. Fenn, and Murnaghan, McGinn and White, in describing the typical picture of pulmonary embolism, pointed out the difficulty that is sometimes encountered in the differentiation of the pain of pulmonary embolism and that of myocardial infarction, the typical picture of both being "sudden severe pain in the chest associated with circulatory collapse." They indicated that the typical pleural pain usually did not appear until some hours later, when a pleural friction rub was often present. This pleural pain may be located in either side of the chest, in the back, or in the shoulder, if the diaphragmatic portion of the pleura is involved. There are many other reports in the literature which describe pain associated with pulmonary embolism, but there are few which distinguish clearly the two different types of pain that were delineated by the authors cited above.

It should be re-emphasized that pulmonary embolism and pulmonary infarction are not synonymous terms. Pulmonary embolism produces pain resembling that of myocardial infarction, while pulmonary infarction produces pain resembling that of acute infectious pleuritis. When, as is often the case, embolism is not followed by infarction, only the first type of pain occurs. The pain produced by pulmonary embolism appears to be identical in character and mechanism with that caused by other disorders which cause elevation of pressure in the pulmonary artery. This point is illustrated by the case histories to be presented.

**ILLUSTRATIVE CASES**

Most of the patients whom we have thought to be suffering from pain as the result of pulmonary hypertension have had either (1) lesions of the mitral valve; (2) certain congenital anomalies of the heart; (3) primary diffuse disorders of the lungs, especially asthma and emphysema; or (4) disorders of the pulmonary artery and, more particularly, embolism. In many instances there has been no proof of the diagnosis, and the decision that the pain was induced by pulmonary hypertension rather than by coronary disease has rested on opinion rather than on conclusive evidence. The cases cited below were selected for presentation either because autopsy confirmation was available, or because the clinical evidence seemed reasonably conclusive. In order to conserve space, only the most pertinent data are presented in the following case reports.

**Case 1.** W. A., a 77 year old white man, was admitted to the hospital with the following history:

One week before admission, while sitting in a chair at about 10:00 P.M., he noted severe precordial pain, became dyspneic and cyanotic, and in a few seconds slumped from the chair unconscious. His breathing was stertorous and cyanosis was marked. The following morning he could be aroused but was irrational, and continued so until admission.

![Fig. 1](http://circ.ahajournals.org/)

**FIG. 1.** The record was interpreted as being compatible with myocardial infarction. Postmortem examination proved this to be untrue. Instead, there was marked dilatation of the right side of the heart and a striking dilatation of the pulmonary artery and its branches.

He had complained of precordial pain on exertion, and occasionally at rest, for the year preceding the present episode.

Physical examination revealed a senile, irrational, cyanotic white man with Cheyne-Stokes respiration. The lungs were clear except for fine moist rales at both bases, posteriorly. The blood pressure was 150/80; the pulse was grossly irregular, with a precordial rate of 82 and a radial rate of 70. Precordial
pulsations were prominent, extending from the third to the sixth intercostal space. The area of cardiac dullness extended from the anterior axillary line to the right border of the sternum. The heart sounds were loud. A loud, harsh murmur was heard throughout systole. It was loudest over the apex but was heard with diminishing intensity over the entire precordium, and radiated into the left axilla. During the phases of apnea, a diastolic murmur could be heard in the third and fourth intercostal spaces in the midclavicular line. The quality of this murmur was midway between the rumbling diastolic murmur of mitral stenosis and the blowing diastolic murmur.

Fig. 2. In the center of the photograph the markedly dilated pulmonary artery is held open by a glass rod.

The radial pulses were not palpable. Death occurred less than five minutes after the onset of this final seizure.

Postmortem findings revealed a markedly dilated and moderately hypertrophied right ventricle, with striking dilatation of the pulmonary artery (fig. 2) and of its main branches extending into the lesser divisions to the periphery of each lung. There was only moderate sclerosis of the pulmonary vessels. The right pulmonary vein entered the right auricle. The commissures of the pulmonary valve were separated and the intervening space was occupied by a thin fenestrated membrane. There was an interauricular septal defect 2 cm. in diameter, located in the upper posterior portion of the septum. There was one small calcified plaque in the posterior leaflet of the mitral valve. The coronary vessels were patent throughout. There was no scarring of the myocardium.

Comment. Although the history was incomplete, there was a story of recurrent attacks of precordial pain often brought on by effort, and occasionally occurring at rest. A more severe and prolonged attack was accompanied by cyanosis, dyspnea, and loss of consciousness. The electrocardiogram was interpreted as being compatible with the diagnosis of myocardial infarction. Thus the clinical picture resembled that of coronary disease, but the necropsy revealed no evidence either of coronary disease or of myocardial infarction. The findings were those of congenital defects of the pulmonary veins, interauricular septum, and pulmonary valve, leading to enlargement of the right ventricle and pulmonary vessels. Presumably, the systolic pressure was markedly elevated in the pulmonary artery.

Case 2. A 72 year old white man for four years had had severe paroxysms of bronchial asthma. Shortly after the beginning of the asthma he developed chest pain. This was substernal in location, aching and occasionally cramping in character, and lasted from a few minutes to several hours. The pain came only with severe asthmatic paroxysms, and invariably lasted until relief from the asthmatic attack. Nitroglycerin produced an incomplete relief from pain only to the extent that it relieved the dyspnea.

Physical examination made during an asthmatic attack revealed the patient to be lying flat in bed with inspiratory retraction of the supraclavicular and suprasternal areas with prolonged expiration. Eye grounds revealed grade I arteriosclerotic changes. There was a marked increase in the antero-posterior diameter of the chest, so that it was typically barrel-shaped. The chest was hyperresonant
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throughout. During a paroxysm, voice sounds were obscured completely by high-pitched sibilant rales heard all over the chest. Blood pressure was 150/100; pulse 78, with frequent premature beats. The point of maximum impulse could not be felt and percussion was unsatisfactory because of emphysema. The heart sounds were faint and almost replaced by a moderately loud, harsh systolic murmur. The murmur was loudest at the apex and was transmitted, but was also heard over the aortic area where it was of slightly lower pitch. The asthma was helped by adrenaline when mild, and relieved by aminophylline when severe. When the dyspnea improved the pain, likewise, subsided.

Electrocardiogram revealed multiple premature beats of ventricular origin, left axis deviation, inversion of T waves in leads II and III, and deep QRS complexes in precordial leads I, II, and IV. Chest x-ray films revealed fibrotic changes throughout both lung fields.

Death occurred after 15 months in the hospital. Necropsy revealed marked dilatation and hypertrophy of the right auricle and right ventricle, and dilatation of the pulmonary conus. There was minimal cirrhosis of the liver, and chronic cholecystitis without stones. There were no abnormalities of the coronary arteries, and the myocardium was normal except for hypertrophy and dilatation, as noted above.

Comment. This patient was considered to have had an old myocardial infarction on the basis of the history and the electrocardiogram. However, the autopsy revealed no evidence of infarction or coronary artery disease. The relationship of the pain to the dyspnea and the response to drugs (little or no relief from nitroglycerin; marked benefit from adrenaline and aminophylline) were typical of the pulmonary hypertensive pain associated with bronchial asthma.

Case 3. N. H., a 77 year old Negro man, entered the hospital for the first time on August 8, 1948 because of a slow urinary stream, dribbling of urine for one week, and retention of urine for 48 hours.

Physical examination was negative except for a very large prostate gland. On August 9, a prostatectomy was done, with removal of 78 Gm. of prostatic tissue. The patient remained in bed until August 12, at which time he began to be up and about. On August 18, at 7:30 A.M., the patient collapsed in the bathroom. He was found on the floor unconscious and dyspneic, and the pulse was absent. At 8:00 A.M. he was breathing rapidly and shallowly. The pulse was weak and irregular, with a rate of 100. The blood pressure was 100/60. The patient was covered with sweat. The lungs were clear. Cardiac examination revealed the second pulmonic to be much louder than the second aortic sound.

A short time later the patient said that he was experiencing a constant, pressing, severe substernal pain that radiated to his left shoulder and left arm. The pain persisted for about three hours. Morphine, oxygen, papaverine, heparin, and dicumarol were administered.

Electrocardiographic changes in the next 24 hours were interpreted as being compatible with an acute subendocardial anteroseptal myocardial infarction. The patient improved and it was thought that he was progressing favorably when on August 21, three days later, he was found dead.

Necropsy revealed thrombophlebitis of the right femoral vein and massive pulmonary embolism. There was benign prostatic hypertrophy, cortical necrosis and arteriolar nephrosclerosis. The coronary vessels were widely patent and no abnormalities were observed. There was no evidence of myocardial infarction.

Comment. The clinical findings were compatible with myocardial infarction and the electrocardiogram was so interpreted. Necropsy revealed pulmonary embolism without evidence of disturbance in the coronary circulation or myocardium. This patient illustrates the difficulty in differentiating pain associated with pulmonary hypertension from that associated with coronary disease.

Case 4. O. H. F., a 48 year old white man, was admitted to the hospital on May 27, 1947, complaining of shortness of breath of five years' duration, and pain in the chest of four years' duration. The patient had developed a chronic cough 10 years previously.

In 1942 he developed pain in the right parasternal area. (He had known since 1918 that his heart was on the right side.) The pain was described as having a sharp, tearing, and squeezing quality. It usually followed several hours of exertion, was associated with severe dyspnea, and usually persisted for one to two hours, but occasionally lasted several days. It was definitely aggravated by deep breathing, being especially worse on inspiration. Nitroglycerin produced no relief from the pain. As his dyspnea improved, the pain always diminished in intensity. The pain was nonradiating.

Physical findings revealed a 48 year old man lying flat in bed, in no distress. Optic fundi showed only slight narrowing of the vessels, with no arteriovenous nicking. The chest was full but not barrel-shaped. The right hemithorax was considerably fuller than the left, measuring 5 cm. greater. The lung fields were clear. The vital capacity was 4 liters. The blood pressure was 162/92. Examination revealed the heart
to be more on the right side than on the left. No other abnormalities were noted.

X-ray study revealed the heart to be mainly on the right side. The vessels occupied the position of a normal left-sided heart. There was also a bilateral emphysema, mainly in the lower lobes. The apical pleura was thinned bilaterally.

Angiocardiograms indicated that the chambers of the heart were in the positions which they would occupy if a normal left-sided heart had been pulled over into the right hemithorax mechanically. Lipiodol bronchograms showed no evidence of bronchial dilatation. Electrocardiogram revealed inverted T waves in lead I.

Comment. Aside from emphysema, this patient had displacement and rotation of the heart due to an unknown cause. It seems probable that these conditions were capable of elevating the pressure in the pulmonary artery. The similarities and differences between the pain of this patient and that in angina pectoris are noteworthy.

Case 5. L. B. H., a white woman aged 77, complained of precordial and substernal aching and tightness for 18 years. This was at first noted only on climbing hills, and would disappear quickly when resting.

She was first examined when she was 52 years of age. At that time there were no complaints other than chronic cough. She had no pain or dyspnea, although she was leading an unusually active vigorous life, including long walks up and down steep hills. At the age of 30 she had had an acute attack of polyarthritis with fever. Examination at that time revealed questionable slight cardiac enlargement and a moderately loud (grade III) apical systolic murmur, heard well out into the axilla. Electrocardiograms displayed no abnormality. The pulmonic second sound was exaggerated.

At age 58 she began to note precordial and substernal aching and tightness. This occurred at first only when she would climb steep hills, and would disappear within two or three minutes when she would stand still. Physical examination was essentially unchanged except that the previously normal blood pressure was now slightly elevated (165/102). The electrocardiogram displayed a tendency toward right axis deviation when compared with the record taken six years previously. X-ray study revealed no significant change other than minimal enlargement and a "mitral shape." During the subsequent 18 years, the exertional pain remained essentially unchanged but occurred less frequently as the degree of activity was gradually decreased as the result of advancing age. The patient gradually noted that the pain would occur when at rest, and more readily in the recumbent position. Anxiety and emotional stress tended to induce it, and the discomfort, while not severe, would last for hours. It was also noted that the distress might endure for several days when acute exacerbations of the chronic bronchitis occurred. Nitroglycerin was taken on numerous occasions, the effects of which were uncertain. At times the pain was unaffected. On other occasions it seemed to disappear more rapidly with than without the drug. The dramatic response that commonly occurs in patients with angina pectoris was not observed. During the entire 25 year period, numerous electrocardiograms were taken. None showed evidence of myocardial ischemia. The systolic murmur gradually became somewhat fainter, and an apical diastolic rumble appeared. At age 77 auricular fibrillation and congestive failure first appeared. Prompt improvement followed digitalization.

Comment. The pain was at first interpreted as angina pectoris. With the passing of years this diagnosis became progressively more untenable, and it now appears altogether likely that pulmonary hypertension, secondary to disease of the mitral valve, was the underlying mechanism. It is noteworthy that chronic nonproductive cough was the most conspicuous symptom.

Case 6. P. W., a 67 year old white man, a construction engineer, was seen in 1951 because of a severe upper respiratory infection and because of being awakened at night "fighting for breath."

Since the age of 21 this patient had been constantly exposed to dust in his occupation.

In 1940 he had an episode of swelling of the feet and ankles which was relieved by some large tablets. It was about this time that he began to notice that less effort than usual made him short of breath.

In 1945, having contracted an upper respiratory infection, the patient noticed an episode of squeezing substernal discomfort associated with marked dyspnea while climbing stairs. The dyspnea and the squeezing discomfort were both relieved after a few minutes of rest. The substernal oppression did not radiate and its intensity was directly proportional to the dyspnea. The patient saw his physician and was hospitalized; he was found to have fairly marked pulmonary fibrosis and emphysema, and mild hypertension.

More recently he had noticed on several occasions, a substernal squeezing discomfort and dyspnea on exertion, and both had always been relieved by rest. Both of these symptoms were exacerbated with episodes of upper respiratory infection. He had been awakened at night on several occasions very short of breath, with a feeling that death was imminent. This would necessitate his getting out of bed, going to a window, and being up most of the
rest of the night. He was finally digitalized and enjoyed marked improvement in symptoms.

The present episode followed a week without digitalis, plus the fact that the patient had contracted an upper respiratory infection which had become quite severe.

Physical examination revealed the patient to be quite dyspneic, very nervous, and drenched with sweat. His blood pressure was 190/120, pulse 120, respiration 32 and temperature 102.6 F. The fundi revealed grade II retinopathy. The neck veins were distended. The chest was increased markedly in its anteroposterior diameter. There was a marked right kyphoscoliosis with a typical pigeon-breast shape anteriorly. Dullness was noted posteriorly on both sides extending from the bases upward to the inferior angle of the scapulae. There was hyperresonance to percussion over the entire anterior chest. Bubbling rales were present at both bases, posteriorly. There were fine crackling moist rales and increased breath sounds in the region of the right middle lobe.

The point of maximum cardiac impulse was both thrusting and diffuse, being most prominent in the fifth left intercostal space in the midclavicular line. It was easily seen and felt in the fifth left intercostal space all the way to the sternum. The right border of cardiac dullness was thought to extend 2 to 3 cm. to the right of the sternum. There was a faint apical systolic murmur and a well marked protodiastolic gallop which changed to a double gallop with inspiration. The liver was palpable 2 fingerbreadths below the right costal margin, and was smooth and nontender. Minimal pitting pretibial edema was present. Peripheral pulses were equal and easily palpable.

The patient was digitalized, given aminophylline suppositories, 0.5 Gm. every six hours, and 300,000 units of penicillin every 24 hours for three days. The improvement was uneventful.

Electrocardiogram (fig. 3) revealed evidence of both right and left ventricular hypertrophy and intraventricular block. Exercise to the point of severe dyspnea and substernal discomfort did not change the appearance of the electrocardiogram. Nitroglycerin did not change the electrocardiogram and did not increase exercise tolerance.

The impression was right middle lobe pneumonia superimposed upon chronic pulmonary fibrosis and emphysema, with hypertension and mild acute pulmonary edema on an already existing chronic cor pulmonale. The substernal pain was thought to be due to pulmonary hypertension with distention of the pulmonary artery.

Comment. This patient had the typical story of pain brought on by exertion and relieved in a few minutes by rest. This story and the electrocardiographic findings could very easily be interpreted as being due to coronary artery disease. However, the set-up of chronic pulmonary disease with substernal distress related so closely to the episodes of dyspnea, the evidence of right ventricular enlargement with cor pulmonale, and the failure of nitroglycerin to have a beneficial effect, would lend support to the diagnosis of pain due to pulmonary hypertension.

Discussion

It is apparent, from the foregoing case histories, that patients with pulmonary hypertension may have pain which is very similar to that produced by disease of the coronary arteries. In so far as location, radiation, qual-

![Fig. 3. The record is interpreted as pointing toward hypertrophy of both left and right ventricles. There is also an intraventricular conduction defect. It did not change after exercise sufficient to produce this patient's pain. A record identical with this was obtained five and 10 minutes after nitroglycerin. Nitroglycerin did not prevent the patient's pain nor did it increase his exercise tolerance.](image-url)
ity, and intensity of the pain are concerned, the two types of pain seem to be identical. There are additional features of the syndrome which enhance the difficulty of differentiating these disorders. Thus some of the patients with pulmonary hypertensive pain (for example, cases 5 and 6) complain of pain brought on by physical exertion, and relieved within a few minutes by rest. Other patients have prolonged bouts of pain enduring for several hours or days, and associated with electrocardiographic changes (cases 1, 2, and 4). It is not surprising that the mistaken diagnosis of coronary arteriosclerosis is usually made in these patients. We, ourselves, have repeatedly made this error, and have treated a number of these patients for several years for supposed diseases of the coronary arteries. Further experience has convinced us that the differentiation, while often difficult and occasionally impossible, can usually be made with accuracy if one is aware of the various clinical features of the syndrome of pulmonary hypertensive pain.

The most important clue to the diagnosis comes from the recognition of the existence of a condition capable of causing pulmonary hypertension, and the realization that such disorders may produce a type of chest pain which mimics closely that due to coronary disease. The most common underlying disorders are: (1) lesions of the mitral valve, usually stenotic, but occasionally regurgitant; (2) primary diffuse disorders of the lungs, especially asthma, emphysema, and bronchiectasis; (3) disorders of the pulmonary arteries, of which embolism is the most frequent; and (4) those congenital malformations of the heart which lead to elevation of pressure in the pulmonary artery. In the latter connection, it is of interest to note that, as would be expected because of pulmonary stenosis and actually a low pulmonary arterial pressure, this pain has not been noted in subjects with the tetralogy of Fallot. On the other hand, it has been repeatedly encountered in patients with auricular septal defects, the Eisenmenger complex, and patent ductus arteriosus.

Not all patients with these several disorders complain of pain. On the contrary, it is absent in the majority of instances. It is, likewise, rarely (if ever) encountered in patients with pulmonary hypertension secondary to left ventricular failure. Whether its absence or presence is dependent on the degree of pulmonary hypertension, or on other factors, is uncertain at present. The important point in diagnosis is the realization that any disorder which is capable of causing pulmonary hypertension may produce pain and to demand unequivocal evidence before considering such a patient as having coronary disease.

Aside from objective clinical and roentgenologic evidence of the presence of an underlying disease process which is capable of causing elevation of the pulmonary pressure, there are certain other features which serve as guides in differentiating the pain associated with pulmonary hypertension from that accompanying coronary disease. These are:

1. A history of long-standing cough. This is present in many of the patients, but by no means all of them.

2. Cyanosis, either persistent or intermittent, and usually present during the episodes of pain. Since patients with angina pectoris or myocardial infarction usually exhibit either pallor or no change in color during the episodes of pain, the presence of cyanosis is of diagnostic value. Unfortunately, cyanosis is not always present during the episodes of pulmonary hypertensive pain.

3. Association of the pain with dyspnea. This is a frequent but not a constant feature. Many patients with coronary disease also have dyspnea when they have pain. Most do not, however. It is interesting to note what Heberden said in his description of angina pectoris. "In all other respects, the patients are, at the beginning of this disorder, perfectly well, and in particular have no shortness of breath, from which it is totally different." The presence of typical asthmatic wheezing in a patient with chest pain is a diagnostic clue, provided one can be sure that the underlying disorder is bronchial rather than cardiac asthma.

The dyspnea occurring in patients with pulmonary hypertensive pain is usually of the pulmonary rather than the cardiac type. For
dyspnea of given severity, the vital capacity is likely to be more markedly decreased in the pulmonary than in the cardiac type. Furthermore, the circulation time through the lungs is often normal or only slightly prolonged, except when lesions of the mitral valve are responsible for the pulmonary hypertension.

4. The presence of pain on breathing. This is very unusual in patients with angina pectoris, but is not rare in the presence of myocardial infarction, and particularly when there is an associated pericarditis. As has already been emphasized, those patients with pulmonary embolism who develop infarction of the lung usually have a second type of chest pain. This is of pleural origin, with typical respiratory aggravation. Unlike the pain of pulmonary embolism, which is usually situated in the substernal, precordial, or arm areas, the pain of pleuritis is likely to be maximal in the lateral or posterior areas of the chest. Aside from pulmonary embolism, many of the various other conditions which cause pulmonary hypertension are accompanied by recurrent attacks of pleuritis. Thus the presence of two different types of chest pain, one of which is markedly aggravated by breathing, constitutes evidence against coronary disease and in favor of pulmonary hypertension.

Aside from the respiratory aggravation associated with the typical pleural pain, there is another feature which has been observed in some of our patients. This consists in a slight inspiratory increment in the pulmonary hypertensive pain itself. This is presumably due to the increased flow of blood into the chest during inspiration, and a consequent rise in pulmonary pressure. The degree of increase in the pain has been slight, and information has been elicited only on careful questioning. The phenomenon has not been a constant finding, but its presence may be of value in the differentiation from angina pectoris.

5. Variability of duration of pain. In the vast majority of patients with coronary disease, the pain falls into one of three categories as regards duration: (a) pain lasting a few minutes only, induced by exercise and relieved by rest (angina pectoris); (b) pain lasting 30 minutes or longer, occurring in repeated attacks, usually during recumbency, and soon leading to a fatal issue or to a typical clinical picture of myocardial infarction (status anginosus); (c) pain lasting several hours to several days and then disappearing completely (myocardial infarction). All of these duration patterns may occur in the pain of pulmonary hypertension. However, the latter pain presents itself in additional varieties, which are rarely encountered in patients with coronary disease. Thus a patient with mitral stenosis or congenital cardiac disease may have a steady substernal feeling of distention enduring for weeks or months, with or without aggravation upon exercise. An individual with status asthmaticus may have pain as long as the paroxysms endure. The presence of a pain identical in location and quality with that produced by coronary disease, but failing to conform to the usual duration patterns of the pain of the latter disorder is, therefore, an indication to consider pulmonary hypertensive pain as a possible cause.

6. Clinical evidence of right ventricular hypertrophy. This is one of the most valuable differential points. In the absence of those disorders, such as thyrotoxicosis or anemia and severe anxiety states, which lead to increase in cardiac output, the presence of diffuse forceful pulsations over the whole left precordial area constitutes strong evidence for right ventricular enlargement. In patients with thin chest walls and without dyspnea, it is our impression that this simple clinical phenomenon is likely to be more reliable than electrocardiographic or roentgenologic evidence. Conspicuous evidence of right ventricular enlargement is rare in patients with pain due to coronary disease. Such patients usually present either no signs of cardiac enlargement, or the forceful, heaving, localized apical impulse of left ventricular hypertrophy. Thus simple inspection and palpation of the chest wall will frequently furnish information of crucial importance in the differential diagnosis of the cause of the pain.

7. Electrocardiographic changes may or may not be present in patients with pulmonary hypertensive pain. Thus their absence, while of no value in excluding angina pectoris, con-
stitutes evidence against myocardial infarction as the cause of the pain. When present in patients with pulmonary hypertensive pain, the electrocardiographic changes usually follow the patterns described in patients with acute cor pulmonale following pulmonary embolism. 2, 14, 17, 18 For details concerning the electrocardiographic changes the reader is referred to these publications. It is sufficient here to emphasize that: (1) The electrocardiographic changes are usually those of right axis deviation or right ventricular strain. (2) T-wave alterations suggestive of posterior infarction are not unusual, and occasionally changes suggestive of anterior infarction are seen. (3) Changes characteristic of myocardial infarction may occur because the conditions may coexist. 17 (4) Many of the patients display no characteristic changes. Thus electrocardiograms may be useless or very helpful in differentiating pain associated with pulmonary hypertension from that due to coronary disease. Unless interpreted with extreme care, they may be actually misleading, and may be responsible for an erroneous diagnosis of myocardial infarction. (See electrocardiogram with cases 1 and 6. A diagnosis of coronary occlusion was made in case 1.) This has happened in a number of patients observed personally.

8. Evidence of tissue destruction (fever, leukocytosis, rapid sedimentation rate) occurs in patients with pulmonary hypertensive pain only when there is coexistent infarction or infection of the lungs. The presence of such evidence is, therefore, of value in excluding angina pectoris; the absence of such evidence may be of crucial importance in excluding myocardial infarction.

9. The effect of oxygen. Striking relief of pain as the result of oxygen inhalation speaks for pulmonary hypertensive pain; slight or no relief may be encountered either with this type of pain, or with that due to coronary disease.

10. The effect of drugs may be of crucial importance in diagnosis. Adrenaline may induce or aggravate the pain of coronary disease; it tends to relieve pulmonary hypertensive pain when bronchial asthma is the underlying disease process. Unfortunately, adrenaline is dangerous in patients with coronary disease, and thus its usefulness in differential diagnosis is limited.

Aminophylline may relieve either pain upon intravenous administration. In our experience, relief following rectal or oral administration is more likely to occur when the pain is associated with pulmonary hypertension than with coronary disease.

Nitroglycerin has either no effect or only a minimal palliative effect on pulmonary hypertensive pain. This does not aid in differentiating the syndrome from myocardial infarction but is of great importance in excluding effort angina or status anginosus. We have followed a number of individuals who were diagnosed 15 or 20 years ago as having angina pectoris, but who obtained little or no relief from nitroglycerin. Most of these subjects are now recognized as having pulmonary hypertensive pain, and we believe that our original diagnosis of angina pectoris was incorrect. At the present time we are unwilling to make a positive diagnosis of angina pectoris in the absence of evidence of striking benefit from nitroglycerin.

The points which have been mentioned will usually suffice to allow an accurate differentiation between the pain associated with pulmonary hypertension and that due to coronary disease, in spite of the great similarity of the two conditions. Such a differentiation cannot be made quickly, and especially not by the usual brief clinical examination followed by electrocardiograms. The distinction depends rather upon judicious interpretation of a meticulously conducted examination, and especially upon thoroughness in history taking.

The prognosis in patients with pulmonary hypertensive pain appears to be much better than that in subjects with coronary disease. Sudden unexpected death may occur in subjects with pulmonary embolism, and in those with marked arterial anoxia, but it is less likely to occur than in patients with coronary disease. Frequent, severe, and prolonged attacks of pain have a less ominous significance than in the case of coronary disease. In general, the prognosis is that of the underlying causative disorder. The treatment,
likewise, is essentially that of the underlying disease. In addition, oxygen and rectal aminophylline often are beneficial.

When we turn from the clinical to the physiologic aspects of this syndrome, a number of interesting points arise:

1. Why is the pain so similar to that produced by disorders of the coronary circulation? The answer would appear to be that the afferent nerves from the pulmonary artery enter the nervous system by way of the same pathways as those from the heart. The rich networks of nerve fibers in the pulmonary artery pass to the anterior and posterior pulmonary plexuses, and thence by way of the vagi and the upper four dorsal sympathetic routes to the central nervous system. The identical pathways are followed by nerves from the heart. Furthermore, there are many interconnecting fibers between the pulmonary and cardiac plexuses.

2. What is the exact mechanism of the production of the pain? Several theories have been proposed, but none has been definitely established. For a review of them the reader is referred to the report of Burgess and Ellis.1 The presence of the pain in individuals without cyanosis, and its absence in instances of the tetralogy of Fallot, make unlikely the idea that arterial anoxia is responsible. Since it has been shown that anoxia produces constriction of the pulmonary vessels,19, 20 the dramatic benefit produced in some patients by oxygen can perhaps be ascribed to dilatation of pulmonary vessels, and consequent decline in pulmonary pressure.

The concept of decline in coronary blood flow consequent to decline in cardiac output is not compatible with the demonstration by Courmand and co-workers19 of high cardiac output in most instances of cor pulmonale. The idea of reflex coronary constriction is not supported by the direct experiments of Katz,21 by the type of electrocardiographic changes usually encountered, or by the failure of response to nitroglycerin.

The idea that the pain may be the result of pulmonary arteriosclerosis is disproved by its sudden onset following pulmonary embolism.

The concept that this pain represents right ventricular angina, and is the result of mechanical hindrance to systolic coronary flow consequent to increased right intraventricular pressure, is attractive. The chief evidence against it is the failure to respond to nitroglycerin.

It is perhaps more likely that the pain arises in the pulmonary artery itself, and is the direct result of distention of the vessel. The mechanism would, therefore, be somewhat analogous to that of migraine. This hypothesis is supported by the patients in our series. Each of them had clinical evidence of pulmonary hypertension, and the ones who came to necropsy displayed dilatation of the pulmonary artery. In the absence of convincing evidence to the contrary, this hypothesis would seem to offer the simplest and most likely explanation.

3. What is the reason for the striking relationship of the pain to muscular exercise in certain patients? If one accepts the idea that the pain is the result of distention of the pulmonary artery as the result of increased pressure, the studies of Hickam and Cargill22 probably furnish the answer to this question. They found that exercise which produced no rise in pulmonary arterial pressure in healthy subjects led to a well marked rise in persons with emphysema or mitral stenosis.

**SUMMARY**

1. Chest pain associated with increased pulmonary arterial pressure is infrequently discussed in the recent literature. Perhaps the reason for this is that this pain mimics that of coronary disease so closely that it is usually misdiagnosed as angina pectoris or myocardial infarction.

2. This pain, though identical in character and location with the pain of coronary disease, differs in certain other respects. The differentiation from pain due to coronary disease is considered in some detail.

3. Six case summaries are presented and commented upon.

4. Although the mechanism of the pain is not established beyond question, it is believed that distention of the pulmonary artery consequent to pulmonary hypertension is the most
likely cause. Evidence for this conclusion is presented.

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WILLIAM N. VIAR and T. R. HARRISON

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